Attorney's Docket No.: 119361-00003 / 601B

OIPE IAP9 MAY 08 2008 PATENT & TRADEMARK OFFICE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: McDonald et al.	Art Unit	: 1647
Patent No.	: 7,157,418	Examiner	: Landsman, Robert S.
Issue Date	: January 2, 2007	Conf. No.	: 3887
Serial No.	: 09/360,242	Cust. No.	: 77202
Filed	: July 22, 1999		

Title : METHODS AND COMPOSITIONS FOR TREATING SECONDARY TISSUE DAMAGE AND OTHER INFLAMMATORY CONDITIONS AND DISORDERS

Attn.: Certificate of Corrections Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Dear Sir:

Transmitted herewith are a Request for a Corrected Certificate of Correction (2 pages), Hand-Annotated Sheets (6 pages), Listing of Claims for the Preliminary Amendment filed on 10 February 2006 (10 pages), Change of Correspondence Address Application (1 page) and a return postcard for filing in connection with the above-identified application. All errors sought to be corrected were made in printing by the Patent and Trademark Office, and no fee is believed to be due. However, should it be determined that a fee for filing these papers is required, the Commissioner is authorized to charge Deposit Account No. 02-1818, as stated below:

☒ The Commissioner is hereby authorized to charge any fees that may be due in connection with this paper or with this application during its entire pendency to Deposit Account No. 02-1818. A duplicate of this sheet is enclosed.

Respectfully submitted,

Stephanie Seidman
Reg. No. 33,779

Attorney Docket No. 119361-00003 / 601B
Address all correspondence to:
Stephanie Seidman
Bell, Boyd & Lloyd LLP
3580 Carmel Mountain Road, Suite 200
San Diego, California 92130
Telephone: (858) 509-7410
Facsimile: (858) 509-7460
email: sseidman@bellboyd.com
963223/D/1

CERTIFICATE OF MAILING BY "EXPRESS MAIL"
"Express Mail" Mailing Label Number **EM 162116766 US**
Date of Deposit **May 8, 2008**
I hereby certify that this paper is being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 CFR §1.10 on the date indicated above and is addressed to: Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450.

Jon Levy

Attorney's Docket No.: 119361-00003 / 601B

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: McDonald et al.	Art Unit	: 1647
Patent No.	: 7,157,418	Examiner	: Landsman, Robert S.
Issue Date	: January 2, 2007	Conf. No.	: 3887
Serial No.	: 09/360,242	Cust. No.	: 77202
Filed	: July 22, 1999		
Title	: METHODS AND COMPOSITIONS FOR TREATING SECONDARY TISSUE DAMAGE AND OTHER INFLAMMATORY CONDITIONS AND DISORDERS		

Attn.: Certificate of Corrections Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Dear Sir:

Transmitted herewith are a Request for a Corrected Certificate of Correction (2 pages), Hand-Annotated Sheets (6 pages), Listing of Claims for the Preliminary Amendment filed on 10 February 2006 (10 pages), Change of Correspondence Address Application (1 page) and a return postcard for filing in connection with the above-identified application. All errors sought to be corrected were made in printing by the Patent and Trademark Office, and no fee is believed to be due. However, should it be determined that a fee for filing these papers is required, the Commissioner is authorized to charge Deposit Account No. 02-1818, as stated below:

☒ The Commissioner is hereby authorized to charge any fees that may be due in connection with this paper or with this application during its entire pendency to Deposit Account No. 02-1818. A duplicate of this sheet is enclosed.

Respectfully submitted,

Stephanie Seidman
Reg. No. 33,779

Attorney Docket No. 119361-00003 / 601B
Address all correspondence to:
Stephanie Seidman
Bell, Boyd & Lloyd LLP
3580 Carmel Mountain Road, Suite 200
San Diego, California 92130
Telephone: (858) 509-7410
Facsimile: (858) 509-7460
email: sseidman@bellboyd.com
963223/D/1

CERTIFICATE OF MAILING BY "EXPRESS MAIL"
"Express Mail" Mailing Label Number **EM 162116766 US**
Date of Deposit **May 8, 2008**
I hereby certify that this paper is being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 CFR §1.10 on the date indicated above and is addressed to: Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA, 22313-1450.

Jon Levy

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: McDonald et al.	Art Unit	: 1647
Patent No.	: 7,157,418	Examiner	: Landsman, Robert S.
Issue Date	: January 2, 2007	Conf. No.	: 3887
Serial No.	: 09/360,242	Cust. No.	: 77202
Filed	: July 22, 1999		
Title	: METHODS AND COMPOSITIONS FOR TREATING SECONDARY TISSUE DAMAGE AND OTHER INFLAMMATORY CONDITIONS AND DISORDERS		

Attn.: Certificate of Corrections Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CORRECTION TO ISSUED CERTIFICATE OF CORRECTION

Dear Sir:

Patentee respectfully requests that a corrected Certificate of Correction be issued for the above referenced patent. A new error was introduced by the PTO in the Certificate of Correction issued on April 15, 2008. A hand-corrected version of the issued Certificate of Correction for the above captioned patent is attached. Patentee respectfully requests correction of the following error introduced by the PTO:

In claim 31, on page 4 of the issued Certificate of Correction, in line 22 the PTO incorrectly printed "nhibited" instead of –inhibited–. Please correct the spelling error introduced by the PTO by replacing "nhibited" with –inhibited– as correctly recited in then-pending claim 72 (now issued claim 31) of the claim listing of the Preliminary Amendment filed on 10 February 2006. A copy of the claim listing of the Preliminary Amendment filed on 10 February 2006 is provided herewith as evidence.

Patentee respectfully requests correction of this error. The error sought to be corrected was made in printing by the Patent and Trademark Office, and no fee is believed to be due. However, should it be determined that a fee for filing these papers is required, the Commissioner is authorized to charge Deposit Account No. 02-1818.

963235/D/1

CERTIFICATE OF MAILING BY "EXPRESS MAIL"
"Express Mail" Mailing Label Number **EM 162116766 US**
Date of Deposit **May 8, 2008**
I hereby certify that this paper is being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 CFR §1.10 on the date indicated above and is addressed to: Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA, 22313-1450.

Jon Levy

Respectfully submitted,

Stephanie Seidman
Reg. No. 33,779

Attorney Docket No. 119361-00003 / 601B
Address all correspondence to:
Stephanie Seidman
Bell, Boyd & Lloyd LLP
3580 Carmel Mountain Road, Suite 200
San Diego, California 92130
Telephone: (858) 509-7410
Facsimile: (858) 509-7460
email: sseidman@bellboyd.com

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,157,418 B1
APPLICATION NO. : 09/360242
DATED : January 2, 2007
INVENTOR(S) : John R. McDonald and Phillip J. Coggins

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

IN THE TITLE PAGES:

In Item [57] ABSTRACT, line 1 please delete the "a" between "ligand" and "chemokine"

in Item [57] ABSTRACT, please replace "neutrophiles" with --neutrophils--

in Item [56] *References Cited* please add to the list of OTHER PUBLICATIONS --Kreitman and Pastan, *Semin. Cancer Biol.* *6*(5):297-306 (1995).--

in Item [56] *References Cited* please add to the list of OTHER PUBLICATIONS --Kreitman, R.J., et al., Recombinant toxins, *Adv. Pharmacol., 28*:193-219 (1994).--

in Item [56] *References Cited* please add to the list of OTHER PUBLICATIONS --Medh, J.D., et al., *J. Biol. Chem., 270:*536-540 (1995).--

in Item [56] *References Cited* please add to the list of OTHER PUBLICATIONS --Puri, *Toxicol. Pathol. 27*:53-57 (1999).--

in Item [56] *References Cited* please add to the list of OTHER PUBLICATIONS --Sawada, M., et al., *Neurosci. Lett., 160*:131-4 (1993).--

in Item [56] *References Cited* please add to the list of OTHER PUBLICATIONS --Stirpe, F., et al., *J. Biol. Chem., 255*:6947-6953 (1980).--

in Item [56] *References Cited* please add to the list of OTHER PUBLICATIONS --Ugoccioni, M., et al., *J. Exp. Med., 183*:2379-84 (1996).--

in Item [56] *References Cited* please add to the list of OTHER PUBLICATIONS --Zheng, G., et al., *J. Histochem. Cytochem., 42*: 531-42 (1994).--

in Item [56] *References Cited,* in OTHER PUBLICATIONS: in EMBL database ID HS1301003, please replace "(Lingkine)" with --(Lungkine)--

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,157,418 B1
APPLICATION NO. : 09/360242
DATED : January 2, 2007
INVENTOR(S) : John R. McDonald and Phillip J. Coggins

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

in Hesselgesser et al., please replace "Chernokine" with --Chemokine--
in Richmond et al., please replace "chernokine/chernokine receptor" with --chemokine/chemokine receptor--
in Signoret et al., please replace "Chernokine" with --Chemokine--

IN THE SPECIFICATION:

At column 1, line 24, please insert --FIELD OF THE INVENTION The present invention relates to therapeutic compositions and their use in treatment of disease states. More particularly, compounds, compositions and methods for treating disease states associated with proliferation, migration and physiological activity of cells involved in inflammatory responses, including, but not limited to, secondary tissue damage, are provided.--
at column 14, line 43, please replace "FIG. 1 is a schematic drawing" with --FIG. 1A-1C presents schematic drawings--
at column 14, line 56, please insert --(also designated herein pOPL2)-- between "pGEMEX-SAP" and "encoding"
at column 14, lines 59-60, please replace "map of a conjugate MCP-3-AM-Shiga-A1" with --map of a plasmid, designated pOPL1, encoding the conjugate MCP-3-AM Shiga-A1, which was--
at column 14, lines 62-63, please replace "map of a conjugate MCP-1-AM-SAP" with --map of a plasmid, designated pOPL106, encoding the conjugate MCP-1-AM-SAP--
at column 14, lines 65-66, please replace "map of a conjugate MCP3-AM-Shiga-A1" with --map of a plasmid, designated pOPL101, encoding the conjugate MCP-3-AM Shiga-A1--
at column 16, line 56, please delete "ALP,"
at column 32, line 25, please delete "of"
at column 57, line 30, please insert --)-- between "1986" and "."
at column 57, line 51, please replace "Ed." with --ed.--
at column 68, line 56, please replace "MIP-1 alpha" with --MIP-1α--
at column 69, line 13, please insert --which-- between "mice" and "predictably"

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,157,418 B1
APPLICATION NO. : 09/360242
DATED : January 2, 2007
INVENTOR(S) : John R. McDonald and Phillip J. Coggins

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

IN THE CLAIMS:

Please replace Claims 5, 11, 18, 20, 25, 27, 28, 31, 32, 40, 45, 48, 50 and 55 with the following Claims:

Column 201, delete lines 41-50 and insert:
--5. The method of claim 1, wherein the activated, proliferating or migrating immune cells occur in a disorder or disease state that is selected from the group consisting of CNS injury, CNS inflammatory diseases, neurodegenerative disorders, heart disease, inflammatory eye diseases, inflammatory bowel diseases, inflammatory joint diseases, inflammatory kidney or renal diseases, inflammatory lung diseases, inflammatory nasal diseases, inflammatory thyroid diseases, inflammatory responses associated with bacterial or viral infections and cytokine-regulated cancers.--

Column 202, delete lines 24-46 and insert:
--11. The method of claim 1, wherein the conjugate comprises the following components: (chemokine receptor targeting agent)$_n$, (L)$_q$ and (targeted agent)$_m$, wherein: L is a linker for linking the chemokine receptor targeting agent to a targeted agent; chemokine receptor targeting agent is any moiety that selectively binds to a chemokine receptor and effects internalization of the conjugate;

m and n, which are selected independently, are at least 1; and

q is 0 or more as long as the resulting conjugate binds to the targeted receptor, is internalized and delivers the targeted agent;

the resulting conjugate binds to a receptor that interacts with and internalizes a chemokine, whereby the targeted agent(s) is internalized in a cell bearing the receptor; and

when the conjugate contains a plurality of targeted agents, the targeted agents are the same or different, and when the conjugate contains a plurality of chemokine receptor targeting agents, the targeting agents are the same or different.--

Column 202, delete lines 65-67 and insert:
--18. The method of claim 11, wherein the chemokine receptor targeting agent and targeted agent are linked directly via a covalent or ionic linkage.--

Column 203, delete lines 4 and 5 and insert:
--20. The method of claim 19, wherein the linker is a peptide linkage, a polypeptide or a chemical linker.--

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,157,418 B1
APPLICATION NO. : 09/360242
DATED : January 2, 2007
INVENTOR(S) : John R. McDonald and Phillip J. Coggins

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 203, delete lines 23-30 and insert:
--25. The method of claim 22, wherein the chemokine is selected from the group consisting of IL-8, GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin and fractalkine.--

Column 203, delete lines 34-39 and insert:
--27. The method of claim 1, wherein the chemokine receptor is selected from the group consisting of CXCR-1, CXCR-2, CXCR-3, CXCR-4, CXCR-5, CCR-1, CCR-2A, CCR-2B, CCR-3, CCR-4, CCR-5, CCR-6, CCR-7, CCR-8, CX3CR-1, XCR1, Duffy antigen receptor for chemokines (DARC) and CD97.--

Column 203, delete lines 40-44 and insert:
--28. The method of claim 22, wherein the chemokine receptor is selected from the group consisting of DARC, CXCR-1, CXCR-2, CXCR-3, CXCR-4, CCR-1, CCR-2A, CCR-2B, CCR-3, CCR-4, CCR-5, CCR-6, CCR-7, CCR-8, CX3CR-1, and CD97.--

Column 203, delete lines 55-67 and insert:
--31. A method for inhibiting proliferation or migration of activated immune effector cells, comprising contacting immune effector cells with a conjugate that comprises a targeted agent or a portion thereof and a chemokine receptor targeting agent, whereby activation or proliferation of the immune effector cells is nhibited, inhibited
wherein:
the targeted agent or portion thereof is a toxin;
the chemokine receptor targeting agent is a chemokine or a fragment thereof that binds to a chemokine receptor and internalizes the targeted agent; and
the conjugate binds to a chemokine receptor resulting in internalization of the targeted agent in cells bearing the receptor.--

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,157,418 B1
APPLICATION NO. : 09/360242
DATED : January 2, 2007
INVENTOR(S) : John R. McDonald and Phillip J. Coggins

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 204, delete lines 1-19 and insert:

--32. The method of claim 31, wherein the conjugate comprises the following components: (chemokine receptor targeting agent)$_n$, (L)$_q$ and (targeted agent)$_m$,

wherein: L is a linker for linking the chemokine or fragment thereof to a targeted agent;

m and n, which are selected independently, are at least 1; and

q is 0 or more as long as the resulting conjugate binds to the targeted receptor, is internalized and delivers the targeted agent;

the resulting conjugate binds to a receptor that interacts with and internalizes a chemokine, whereby the targeted agent(s) is internalized in a cell bearing the receptor; and

when the conjugate contains a plurality of targeted agents, the targeted agents are the same or different, and when the conjugate contains a plurality of chemokine receptor targeting agents, the targeting agents are the same or different.--

Column 204, delete lines 45-52 and insert:

--40. The method of claim 29, wherein the chemokine is selected from the group consisting of IL-8, GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin, and fractalkine.--

Column 204, delete lines 65-67 and insert:

--45. A method of preparing a candidate compound for treating a disease or disorder involving activated immune cells, comprising:

identifying immune cells that are activated in the disease or disorder;

identifying chemokine receptors expressed on the cells; and

preparing a conjugate or plurality thereof containing a toxin linked to a chemokine or a plurality of chemokines that specifically bind to the identified chemokine receptors and effect or facilitate internalization of the toxin into the cells.--

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,157,418 B1
APPLICATION NO. : 09/360242
DATED : January 2, 2007
INVENTOR(S) : John R. McDonald and Phillip J. Coggins

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 205, delete lines 16-24 and insert:
--48. The method of claim 21, wherein the chemokine receptor targeting agent is selected from the group consisting of IL-8, GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin, and fractalkine.--

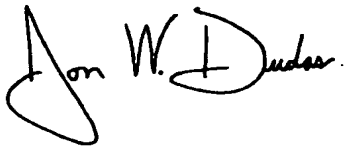
Column 206, delete lines 1-8 and insert:
--50. The method of claim 45, wherein the chemokine is selected from the group consisting of IL-8,GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin, and fractalkine.--

Column 206, delete lines 24-26 and insert:
--55. The method of claim 45, further comprising:
contacting the immune cells with the conjugate or plurality thereof, whereby the toxin is internalized.--

This certificate supersedes the Certificate of Correction issued March 18, 2008.

Signed and Sealed this

Fifteenth Day of April, 2008



JON W. DUDAS
Director of the United States Patent and Trademark Office

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: John R. McDonald et al.	Art Unit	: 1647
Serial No.	: 09/360,242	Examiner	: Robert S. Landsman
Filed	: July 22, 1999	Cust. No.	: 20985
Conf. No.	: 3887		

Title : METHODS AND COMPOSITIONS FOR TREATING SECONDARY TISSUE DAMAGE AND OTHER INFLAMMATORY CONDITIONS AND DISORDERS

MAIL STOP: RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PRELIMINARY AMENDMENT AND REQUEST FOR CONTINUED EXAMINATION (RCE)

Dear Sir:

This preliminary amendment, which is responsive to the Final Office Actions, mailed April 7, 2005 and August 10, 2005, is filed with Request for Continued Examination (RCE) of the above-captioned application. Entry of the following amendments and consideration of the following remarks are respectfully requested.

Amendments to the specification begin on page 2 of this paper.

Amendments to the claims are reflected in the listing of the claims, which begin on page 3 of this paper.

Remarks/Arguments begin on page 11 of this paper.

CERTIFICATE OF MAILING BY "EXPRESS MAIL"
"Express Mail" Mailing Label Number EV738975037US
Date of Deposit: February 10, 2006
I hereby certify that this paper is being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 CFR §1.10 on the date indicated above and is addressed to: Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA, 22313-1450.

Stephanie Seidman

AMENDMENT TO THE SPECIFICATION:

Please amend the specification at page 1, under "Related Application," as lines 4-26 as follows:

This application claims the benefit of priority under 35 U.S.C. §119(e) to U.S. ~~application Serial No. 09/120,523, filed July 22, 1998, and converted to a provisional application on July 22, 1999, serial number unavailable,~~ provisional application Serial No. 60/155,185 by McDONALD, John R. and COGGINS, Philip J., entitled "METHODS AND COMPOSITIONS FOR TREATING SECONDARY TISSUE DAMAGE", filed July 22, 1998, now abandoned. This application is a ———

~~This application also claims the benefit of priority under 35 U.S.C. '120 as a~~ continuation-in-part of International PCT application No. ~~(Attorney Docket No. 25020-601PC)~~ PCT/CA99/00659, filed July 21, 1999, by Osprey Pharmaceuticals Limited, McDONALD, John R. and COGGINS, Philip J. entitled "METHODS AND COMPOSITIONS FOR TREATING SECONDARY TISSUE DAMAGE AND OTHER INFLAMMATORY CONDITIONS AND DISORDERS".

The subject matter of each of U.S. application Serial No. 09/120,523 and of International PCT application No. ~~(Attorney Docket No. 25020-601PC)~~ PCT/CA99/00659 is herein incorporated by reference in its entirety.

AMENDMENTS TO THE CLAIMS:

Please amend claims 29, 68, 81, 72 and 89-91 as follows. This listing of claims replaces all prior versions, and listings of claims, in the application.

LISTING OF CLAIMS:

1-25. (Cancelled)

26. **(Previously Presented)** The method of claim 29, wherein the immune effector cells are leukocytes that express chemokine receptors.

27. **(Previously Presented)** The method of claim 29, wherein the inflammatory response results in secondary tissue damage.

28. **(Previously Presented)** The method of claim 29, wherein the immune effector cells are selected from mononuclear phagocytes (MNP), leukocytes, natural killer cells, dendritic cells, T lymphocytes and B lymphocytes.

29. **(Currently Amended)** A method for inhibiting ~~activation,~~ proliferation or migration of activated immune effector cells, comprising administering a conjugate to an animal, whereby ~~activation,~~ proliferation or migration of the immune effector cells is inhibited, wherein:

the conjugate comprises a targeted agent or a portion thereof and a chemokine receptor targeting agent or a portion thereof sufficient to bind to a chemokine receptor on immune effector cells and facilitate internalization of the conjugate;

the chemokine receptor targeting agent is a chemokine, an antibody that specifically binds to a chemokine receptor or a fragment of the chemokine or antibody, wherein the chemokine, antibody or fragment thereof binds to the receptor and internalizes the targeted agent in a cell;

the targeted agent or portion thereof, when internalized in a cell, alters metabolism or gene expression in the cell, regulates or alters protein synthesis in the cell, inhibits proliferation of the cell or kills the cell; and

the conjugate binds to a chemokine receptor resulting in internalization of the targeted agent in cells bearing the receptor.

30. (Cancelled)

31. **(Previously Presented)** The method of claims 29, wherein the activated, proliferating or migrating immune cells occur in a disorder or disease state that is selected from the group consisting of CNS injury, CNS inflammatory diseases, neurodegenerative disorders, heart disease, inflammatory eye diseases, inflammatory bowel diseases,

inflammatory joint diseases, inflammatory kidney or renal diseases, inflammatory lung diseases, inflammatory nasal diseases, inflammatory thyroid diseases, inflammatory responses associated with bacterial or viral infections and cytokine-regulated cancers.

32. **(Original)** The method of claim 31, wherein the CNS inflammatory diseases and neurodegenerative disorders are selected from the group consisting of stroke, closed head injury, leukoencephalopathy, choriomeningitis, meningitis, adrenoleukodystrophy, AIDS dementia complex, Alzheimer's disease, Down's Syndrome, chronic fatigue syndrome, encephalitis, encephalomyelitis, spongiform encephalopathies, multiple sclerosis, Parkinson's disease, and spinal cord injury/trauma (SCI).

33. (Cancelled)

34. **(Previously Presented)** The method of claim 29, wherein the targeted agent is a toxin.

35. **(Previously Presented)** A method of targeted delivery of an agent into cells that express chemokine receptors, comprising associating the agent with a chemokine receptor targeting agent, whereby:

the chemokine receptor targeting agent binds to a chemokine receptor expressed on the cells; and

the agent is internalized by the cells, wherein the cells are immune effector cells.

36. **(Previously Presented)** The method of claim 35, wherein the immune effector cells are activated leukocytes.

37. **(Original)** The method of claim 27, wherein the secondary tissue damage results from spinal cord injury or trauma.

38-39. (Cancelled)

40. **(Previously Presented)** A method for inhibiting the proliferation, migration or activity of secondary tissue damage-promoting inflammatory cells, comprising administering to a subject in need thereof an effective amount of a therapeutic agent that inhibits the proliferation, migration or physiological activity of secondary tissue damage-promoting inflammatory cells, wherein the therapeutic agent is a conjugate that comprises a chemokine receptor targeting agent and a targeted agent or portion thereof selected so that conjugate binds to a chemokine receptor and internalizes the targeted agent, which inhibits the proliferation, migration or physiological activity of the secondary tissue damage-promoting cells.

41. (Cancelled)

42. **(Previously Presented)** The method of claim 29, wherein the conjugate is selected from the group consisting of OPL98104, OPL98112, OPL98108, OPL98102, OPL98110, OPL98106, OPL98101, OPL98109, OPL98105, OPL98103, OPL98111 and OPL98107.

43. (Cancelled)

44. **(Previously Presented)** The method of claim 29, wherein the conjugate comprises the following components: (chemokine receptor targeting agent)n, (L)q and (targeted agent)m, wherein:

L is a linker for linking the chemokine receptor targeting agent to a targeted agent;

chemokine receptor targeting agent is any moiety that selectively binds to a chemokine receptor and effects internalization of the conjugate;

m and n, which are selected independently, are at least 1; and

q is 0 or more as long as the resulting conjugate binds to the targeted receptor, is internalized and delivers the targeted agent;

the resulting conjugate binds to a receptor that interacts with and internalizes a chemokine, whereby the targeted agent(s) is internalized in a cell bearing the receptor; and

when the conjugate contains a plurality of targeted agents, the targeted agents are the same or different, and when the conjugate contains a plurality of chemokine receptor targeting agents, the targeting agents are the same or different.

45. **(Previously Presented)** The method of claim 44, wherein m and n, which are selected independently, are 1-6.

46. **(Previously Presented)** The method of claim 44, wherein q is 1, n is 2 and m is 1.

47. (Cancelled)

48. **(Previously Presented)** The method of claim 44, wherein the chemokine receptor targeting agent specifically binds to chemokine receptors on activated leukocytes.

49. **(Previously Presented)** The method of claim 44, wherein the chemokine receptor targeting agent specifically binds to chemokine receptors on activated cells selected from mononuclear phagocytes (MNP), leukocytes, natural killer cells, dendritic cells, T lymphocytes and B lymphocytes.

50. **(Previously Presented)** The method of claim 49, wherein the activated leukocytes are selected from basophils, neutrophils, eosinophils or combinations of any two or more thereof.

51. **(Previously Presented)** The method of claim 44, wherein the targeted agent is a toxin, a nucleic acid or a therapeutic protein.

52. **(Previously Presented)** The method of claim 44, wherein the chemokine receptor targeting agent and targeted agent are linked directly via a covalent or ionic linkage.

53. **(Previously Presented)** The method of claim 44, wherein the chemokine receptor targeting agent and targeted agent are joined via a linker.

54. **(Previously Presented)** The method of claim 53, wherein the linker is a peptide linkage, a polypeptide or is chemical linker.

55-56. (Cancelled)

57. **(Previously Presented)** The method of claim 44, wherein the chemokine receptor targeting agent is a chemokine or a fragment thereof that binds to the receptor and internalizes the targeted agent.

58-64. (Cancelled)

65. **(Previously Presented)** The method of claim 29, wherein the chemokine receptor targeting agent is a chemokine or a sufficient portion thereof to specifically bind to a chemokine receptor and to facilitate internalization of the conjugate.

66. **(Previously Presented)** The method of claim 29, wherein the chemokine targeting agent is a chemokine that is a member of the superfamily of chemokines that interact with at least one of the chemokine receptors selected from the group consisting of the CC-, CXC-, CX3C- and XC-receptors.

67. **(Previously Presented)** The method of claim 29, wherein the chemokine targeting agent is a chemokine that is a member of the superfamily of chemokines that interact with at least one of the chemokine receptors selected from the group consisting of the CC- and CXC- receptors.

68. **(Currently Amended))** The method of claim 65, wherein the chemokine is selected from the group consisting of IL-8, GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, ~~PF4,~~ IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin and fractalkine.

69. **(Previously Presented)** The method of claim 65, wherein the chemokine is selected from the group consisting of lungkine, ALP, Tim-1, chemokine α-5, chemokine α-6 and chemokine β15.

70. **(Previously Presented)** The method of claim 29, wherein the chemokine receptor selected from the group consisting of CXCR-1, CXCR-2, CXCR-3, CXCR-4, CXCR-5, CCR-1, CCR-2A, CCR-2B, CCR-3, CCR-4, CCR-5, CCR-6, CCR-7, CCR-8, CCR-8, CX3CR-1, XCR1, Duffy antigen receptor for chemokines (DARC) and CD97.

71. **(Previously Presented)** The method of claim 65, wherein the chemokine receptor is selected from the group consisting of DARC, CXCR-1, CXCR-2, CXCR-3, CXCR-4, CCR-1, CCR-2A, CCR-2B, CCR-3, CCR-4, CCR-5, CCR-6, CCR-7, CCR-8, CX3CR-1, and CD97.

72. **(Currently Amended)** A method for inhibiting ~~activation,~~ proliferation or migration of activated immune effector cells, comprising contacting immune effector cells with a conjugate that comprises a targeted agent or a portion thereof and a chemokine receptor targeting agent, whereby activation~~,~~ or proliferation~~, migration~~ of the immune effector cells is inhibited, wherein:

the targeted agent or portion thereof is a toxin;

the chemokine receptor targeting agent is a chemokine or a fragment of thereof that binds to a chemokine receptor and internalizes the targeted agent; and

the conjugate binds to a chemokine receptor resulting in internalization of the targeted agent in cells bearing the receptor.

73. **(Previously Presented)** The method of claim 72, wherein the conjugate comprises the following components: (chemokine receptor targeting agent)n, (L)q and (targeted agent)m, wherein:

L is a linker for linking the chemokine or fragment thereof to a targeted agent;

m and n, which are selected independently, are at least 1; and

q is 0 or more as long as the resulting conjugate binds to the targeted receptor, is internalized and delivers the targeted agent;

the resulting conjugate binds to a receptor that interacts with and internalizes a chemokine, whereby the targeted agent(s) is internalized in a cell bearing the receptor; and

when the conjugate contains a plurality of targeted agents, the targeted agents are the same or different, and when the conjugate contains a plurality of chemokine receptor targeting agents, the targeting agents are the same or different.

74. **(Previously Presented)** The method of claim 73, wherein m and n, which are selected independently, are 1-6.

75. **(Previously Presented)** The method of claim 73, wherein q is 1, n is 2 and m is 1.

76. **(Previously Presented)** The method of claim 73, wherein the chemokine specifically binds to chemokine receptors on activated leukocytes.

77. **(Previously Presented)** The method of claim 73, wherein the chemokine specifically binds to chemokine receptors on activated cells selected from mononuclear phagocytes (MNP), leukocytes, natural killer cells, dendritic cells, T lymphocytes and B lymphocytes.

78. **(Previously Presented)** The method of claim 76, wherein the activated leukocytes are selected from basophils, neutrophils, eosinophils or combinations of any two or more thereof.

79. **(Previously Presented)** The method of claim 73, wherein the chemokine is a member of the superfamily of chemokines that interact with at least one of the chemokine receptors selected from the group consisting of the CC-, CXC-, CX3C- and XC-receptors.

80. **(Previously Presented)** The method of claim 73, wherein the chemokine is a chemokine that is a member of the superfamily of chemokines that interact with at least one of the chemokine receptors selected from the group consisting of the CC- and CXC-receptors.

81. **(Currently Amended)** The method of claim 35, wherein the chemokine is selected from the group consisting of IL-8, GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, ~~PF4~~, IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin, and fractalkine.

82. **(Previously Presented)** The method of claim 40, wherein the targeted agent, when internalized in a cell, alters metabolism or gene expression in the cell, regulates or alters protein synthesis in the cell, inhibits proliferation of the cell or kills the cell.

83. **(Previously Presented)** The method of claim 29, wherein the targeted agent is selected from among ribosome inactivating proteins (RIPs) and bacteriocins.

84. **(Previously Presented)** The method of claim 73, wherein the toxin is a ribosome inactivating protein or a toxic subunit thereof.

85. **(Previously Presented)** The method of claim 29, wherein the targeted agent is a toxin that is a ribosome inactivating protein or a toxic subunit thereof.

86. **(Previously Presented)** A method of preparing a candidate compound for treating a disease or disorder involving activated immune cells an inflammatory response, comprising:

identifying immune cells that are activated in the disease or disorder;

identifying chemokine receptors expressed on the cells;

preparing a conjugate or plurality thereof containing toxin linked to a chemokine or a plurality of chemokines that specifically bind to the identified chemokine receptors and effect or facilitate internalization of the toxin into the cells.

87. **(Previously Presented)** The method of claim 86, wherein a plurality of conjugates that bind to a plurality of chemokine receptors are prepared.

88. **(Previously Presented)** The method of claim 29, wherein the chemokine receptor targeting agent is selected from the group consisting of IL-8, GRO-α, GRO-β, IP-10, SDF-1β, MCP-1 MCP-3, eotaxin-1, eotaxin-2 and RANTES.

89. **(Currently Amended)** The method of claim 57, wherein the chemokine receptor targeting agent is selected from the group consisting of IL-8, GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, ~~PF4~~, IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin, and fractalkine.

90. **(Currently Amended)** The method of claim 40, wherein the chemokine receptor targeting agent is selected from the group consisting of IL-8, GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, ~~PF4~~, IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin, and fractalkine.

91. **(Currently Amended)** The method of claim 86, wherein the chemokine is selected from the group consisting of IL-8, GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, ~~PF4,~~ IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin, and fractalkine.

92. **(Previously Presented)** The method of claim 29, wherein the immune effector cells are selected from among monocytes, macrophages, leukocytes and microglia.

93. **(Previously Presented)** The method of claim 44, wherein the immune effector cells are selected from among monocytes, macrophages, leukocytes and microglia.

94. **(Previously Presented)** The method of claim 35, wherein the immune effector cells are selected from mononuclear phagocytes (MNP), leukocytes, natural killer cells, dendritic cells, T lymphocytes and B lymphocytes.

95. **(Previously Presented)** The method of claim 35, wherein the immune effector cells are selected from among monocytes, macrophages, leukocytes and microglia.

96. **(Previously Presented)** The method of claim 86, further comprising:

contacting the immune cells with the conjugate or plurality thereof, whereby the toxin is internalized.

97. **(Previously Presented)** The method of claim 96, wherein a plurality of conjugates that bind to a plurality of chemokine receptors are prepared, and the immune cells are contacted with each of the conjugates simultaneously or sequentially.